

## ABSTRACT

Proteins in the IKK and JNK signaling pathways, such as NF $\kappa$ B, are involved in  
5 the regulation of inflammatory diseases. Through phosphorylation and  
polyubiquitination, I $\kappa$ B proteins which sequester NF $\kappa$ B in the cytoplasm, are degraded  
by the ubiquitin-proteasome pathway releasing NF $\kappa$ B to the nucleus where it is activated.  
The present invention provides methods utilizing the composition of proteins in the IKK,  
JNK and ubiquitin-proteasome pathways such as, TRAF6 or TRAF2 (E3-ubiquitin  
10 protein ligase), TRIKA1/Uev1A/Ubc13 complex (E2-ubiquitin conjugating enzyme), and  
TRIKA2/TAK1 (protein kinase), in screening for candidate modulators involved in  
activation of the IKK and JNK pathways. The application further provides methods of  
utilizing the candidate modulators as drug therapeutics against inflammatory and immune  
diseases.